

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: BEN SACKY Examiner #: 73489 Date: 12/12/02
 Art Unit: 1626 Phone Number 305-6889 Serial Number: 10/066 801
 Mail Box and Bldg/Room Location: CM1 E11 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

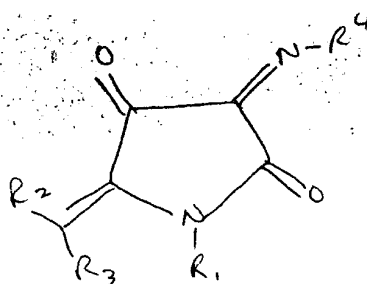
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Substituted Pyrrolidine-2,3,4-Triox-3-Oxime Derivatives

Inventors (please provide full names): Dziewosny et al.

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



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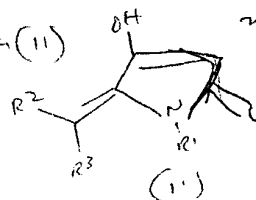
(1)
(STIC)

R₁ is H, OR^R, OH, SR^R, COR^R, COOR^R etc.
 R₂ and R₃ are independently H, F, Cl, Br, CF₃ etc.

R⁴ is H, OH, OR^R, SR^R, COR^R, COOR^R, COLO
 CONR^RR⁷, CS NR^RR⁷ or C₁₋₁₀ alkyl.

and also method of preparing formula (I)

comprising reacting tetramic acid of formula (II) with an aqueous solution of sodium nitrite in an ice-cooled solution.



Point of Contact:
 Barb O'Brien
 Technical Information Specialist
 STIC CM1 6A05 308-4291

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	Type of Search	Vendors and cost where applicable
Searcher: <u>BOOF</u>	NA Sequence (#) _____	STN <u>339</u>
Searcher Phone #: _____	AA Sequence (#) _____	Dialog _____
Searcher Location: _____	Structure (#) <u>4</u>	Questel/Orbit _____
Date Searcher Picked Up: <u>12-18-02</u>	Bibliographic _____	Dr. Link _____
Date Completed: <u>12-18-02</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time: <u>30</u>	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time: <u>13</u>	Other _____	Other (specify) _____

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IFIUDB
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and
ZCAPLUS
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 03 New e-mail delivery for search results now available
NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
saved answer sets no longer valid
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
NEWS 15 Jul 30 NETFIRST to be removed from STN
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NEWS 18 Aug 08 NTIS has been reloaded and enhanced
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
now available on STN
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NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
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NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28 Oct 21 EVENTLINE has been reloaded
NEWS 29 Oct 24 BEILSTEIN adds new search fields
NEWS 30 Oct 24 Nutraceuticals International (NUTRACEUT) now available on
STN
NEWS 31 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 32 Nov 18 DKILIT has been renamed APOLLIT
NEWS 33 Nov 25 More calculated properties added to REGISTRY
NEWS 34 Dec 02 TIBKAT will be removed from STN
NEWS 35 Dec 04 CSA files on STN

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CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),

AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002

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FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 11 DEC 2002 HIGHEST RN 475975-25-8

DICTIONARY FILE UPDATES: 11 DEC 2002 HIGHEST RN 475975-25-8

TS/CA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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FILE COVERS 1907 - 12 Dec 2002 VOL 137 ISS 24
FILE LAST UPDATED: 11 Dec 2002 (20021211/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> e del199365210/pn

E1	1	DE19936520/PN
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E3	0 -->	DE199365210/PN
E4	1	DE19936524/PN
E5	1	DE19936543/PN
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E9	1	DE19936549/PN
E10	1	DE19936552/PN
E11	1	DE19936556/PN
E12	1	DE19936563/PN

=> e del19936521/pn

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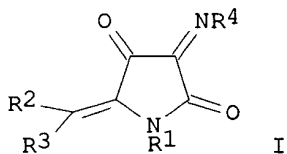
L1 1 DE19936521/PN

=> d 11 all

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
 AN 2001:115115 CAPLUS
 DN 134:162915
 TI Preparation of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists.
 IN Przewosny, Michael; Stachel, Hans-Dietrich; Poschenrieder, Hermann
 PA Grunenthal G.m.b.H., Germany
 SO PCT Int. Appl., 52 pp.
 CODEN: PIXXD2
 DT Patent
 LA German
 IC ICM C07D207-02
 ICS A61K031-4015; A61P025-04; A61P029-00
 CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
 Section cross-reference(s): 1

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001010831	A1	20010215	WO 2000-EP7101	20000725
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19936521	A1	20010215	DE 1999-19936521	19990806 <--
BR 2000013313	A	20020416	BR 2000-13313	20000725
EP 1200400	A1	20020502	EP 2000-945950	20000725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NO 2002000578	A	20020325	NO 2002-578	20020205
PRAI DE 1999-19936521	A	19990806		
WO 2000-EP7101	W	20000725		
OS MARPAT 134:162915				
GI				



AB Title compds. (I; R1 = H, OR8, COR5, NR6R7, CO2R5, CONR6R7, CSNR6R7, alkyl, aryl, heteroaryl, aralkyl; R2, R3 = H, F, Cl, Br, CF3, OR8, SR8, alkyl, aryl, heteroaryl, aralkyl; R4 = OH, H, OR8, SR8, COR5, CO2R5, COCOR5, CONR6R7, CSNR6R7, alkyl, aryl, heteroaryl, aralkyl; R5 = H, alkyl,

aryl, heteroaryl, aralkyl; R6, R7 = H, OR8, COR5, CO2R5, alkyl, aryl, heteroaryl, aralkyl; R8 = alkyl, aryl, heteroaryl, aralkyl), were prepd. 4-Hydroxy-5-(methoxyphenylmethylene)-1,5-dihydropyrrol-2-one in HOAc was treated with NaNO₂ followed by stirring for 30 min. to give 60% 5-(methoxyphenylmethylene)pyrrolidin-2,3,4-trione 3-oxime. The latter bound to the glycine binding site of NMDA receptors with K_i = 0.116

.mu.M.

- ST pyrrolidinetrione oxime prepn NMDA receptor antagonist; analgesic pyrrolidinetrione oxime prepn; antiinflammatory pyrrolidinetrione oxime prepn; antidepressant pyrrolidinetrione oxime prepn; drug abuse treatment pyrrolidinetrione oxime prepn; alcoholism treatment pyrrolidinetrione oxime prepn; cardiovascular agent pyrrolidinetrione oxime prepn; antipsychotic pyrrolidinetrione oxime prepn; antiparkinsonian pyrrolidinetrione oxime prepn
- IT AIDS (disease)
 - (AIDS dementia complex, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Mental disorder
 - (AIDS dementia, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Brain, disease
 - (Gilles de la Tourette syndrome, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Nervous system
 - (Huntington's chorea, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Glutamate antagonists
 - (NMDA antagonists; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Drugs of abuse
 - (abuse of, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Brain, disease
 - (edema, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Stomach, disease
 - (gastritis, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Bladder
 - (incontinence, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Brain, disease
 - (infarction, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Brain, disease
 - (ischemia, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor antagonists)
- IT Analgesics
 - Anti-Alzheimer's agents
 - Anti-inflammatory agents
 - Anticonvulsants
 - Antidepressants
 - Antidiarrheals
 - Antiparkinsonian agents

Antipsychotics
 Antitussives
 Anxiolytics
 Cardiovascular agents
 (prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor
 antagonists)

IT Oximes
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor
 antagonists)

IT Brain, disease
 (stroke, treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA
 receptor antagonists)

IT Respiratory tract
 (treatment of airway disease; prepn. of pyrrolidine-2,3,4-trion-3-
 oximes as NMDA receptor antagonists)

IT Asphyxia
 (treatment of perinatal asphyxia; prepn. of pyrrolidine-2,3,4-trion-3-
 oximes as NMDA receptor antagonists)

IT Alcoholism
 Encephalomyelitis
 Hypoxia, animal
 (treatment; prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA
 receptor
 antagonists)

IT 247901-14-0P 247901-15-1P 247901-16-2P 247901-17-3P 247901-18-4P
 247901-19-5P 247901-20-8P 247901-30-0P 247901-45-7P
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor
 antagonists)

IT 106237-90-5 247901-78-6 247901-79-7 247901-80-0 247901-81-1
 247901-82-2 247901-83-3 247901-84-4 325773-48-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (prepn. of pyrrolidine-2,3,4-trion-3-oximes as NMDA receptor
 antagonists)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE
 (1) Gruenenthal GmbH; EP 0894497 A 1999 CAPLUS
 (2) Pfizer Ltd; WO 9608485 A 1996 CAPLUS
 (3) Poschenrieder; CAPLUS
 (4) Poschenrieder; ARCH PHARM (WEINHEIM, GER) 1998, V331(12), P389 CAPLUS
 (5) Poschenrieder, H; ARCH PHARM 1999, V332(9), P309 CAPLUS
 (6) Rowley, M; TETRAHEDRON 1992, V48(17), P3557 CAPLUS